Updated March 2019

Selected CTEP Clinical Accomplishments

CTEP-sponsored clinical trials provide significant findings that advance the treatment of cancer. Below is a compilation of some of these contributions.

- National Clinical Trials Network

During the first four years of the program (2014-2018), the Network supported 31 practice-changing clinical trials, including:

- RTOG-1016—An interim analysis of data from this randomized, phase 3 clinical trial of patients with human papillomavirus (HPV)-positive oropharyngeal cancer found that treatment with radiation therapy and cetuximab is associated with worse overall and progression-free survival compared to the current standard treatment with radiation and cisplatin. The trial was designed to see if cetuximab with radiation would be less toxic than cisplatin with radiation without compromising survival for patients with the disease.

- TAILORx/PACCT-1—The Trial Assigning Individualized Options for Treatment (Rx), or TAILORx trial, showed no benefit from chemotherapy for 70 percent of women with the most common type of early stage breast cancer. The study found that for women with hormone receptor (HR)-positive, HER2-negative, axillary lymph node–negative breast cancer, treatment with chemotherapy and hormone therapy after surgery is not more beneficial than treatment with hormone therapy alone.

- A091105 (also see NCI Press Release)—The results from this randomized, phase 3 clinical trial for patients with desmoid tumors or aggressive fibromatosis (DT/DF), which are rare tumors, showed that the multi-kinase inhibitor sorafenib tosylate (Nexavar) significantly extended progression-free survival compared with a placebo, making this drug a practice-changing approach for these patients.

- RTOG 0126—For patients with intermediate-risk prostate cancer, this randomized trial compared the efficacy of standard vs dose-escalated radiation therapy, which some clinicians were recommending and using without rigorous scientific evidence. Despite improvements in biochemical failure and distant metastases, dose escalation did not improve overall survival. High doses caused more late toxic effects and lower rates of salvage therapy.

- AALL0434—This largest-ever trial for children and adolescents with newly-diagnosed T-cell acute lymphoblastic leukemia (ALL) showed a disease-free survival rate exceeding 90 percent for patients who were randomized to receive high-dose methotrexate and nelarabine.

- E2211—Presented at ASCO 2018, this prospective, randomized phase 2 study showed that in patients with advanced pancreatic neuroendocrine tumors the combination of temozolomide and capecitabine improved progression-free survival and overall survival compared to temozolomide alone.

- NRG/GOG-0240—Established that long-term overall survival of advanced cervical cancer is improved with the addition of bevacizumab; FDA approval was obtained in 2014.

- CATNON RTOG 0834 (NRG)—International study showed that adjuvant temozolomide chemotherapy was associated with a significant survival benefit in patients with newly diagnosed non-co-deleted anaplastic glioma.

- CALGB 10603—Midostaurin approved by FDA in 2017 for adult patients with newly diagnosed acute myeloid leukemia.

- CALGB 100104—Provided critical contribution for the 2017 FDA approval for lenalidomide as maintenance therapy after autologous transplant for multiple myeloma.

- NRG GOG-0213—Adding bevacizumab to standard chemotherapy for first recurrence platinum-sensitive ovarian cancer showed an overall survival benefit and led to the 2017 FDA licensing of bevacizumab for use in first recurrence of this cancer. It was reported in 2018 that secondary cytoreduction for women with first platinum-sensitive recurrence resulted in no better overall survival, changing practice away from surgery plus chemotherapy to chemotherapy alone.

- ANBL1221—This randomized, phase 2 trial showed that relapsed and refractory neuroblastomas in children had a greater response to the combination of irinotecan-temozolomide-dinutuximab than to irinotecan-temozolomide-temsirolimus. This is a new standard of care for recurrent neuroblastoma. A pilot is underway to see if dinutuximab can be given with induction therapy for newly diagnosed high risk neuroblastoma patients.

- ECOG-ACRIN E3805—Docetaxel given at the beginning of androgen deprivation therapy for metastatic prostate cancer significantly increased overall survival.

- N0574—Among patients with 1 to 3 brain metastases, the use of stereotactic radiosurgery (SRS) alone, compared with SRS plus whole brain radiotherapy, resulted in less cognitive deterioration at 3 months. These findings suggest that for brain metastases amenable to radiosurgery, SRS alone may be a preferred strategy.

- ANBL0531—Standard of therapy became tandem myeloablative autologous stem cell transplant using peripheral blood stem cells for high-risk neuroblastoma.

- COG AALL0232—In pediatric patients with high-risk acute B cell lymphoblastic leukemia, event-free survival increased with the use dexamethasone (compared with prednisone) and high-dose methotrexate (compared to an alternative way of administering methotrexate).

- CAN-NCIC-MA17R—In early-stage breast cancer, 10 years of aromatase inhibitor therapy improved disease-free survival when compared to five years of therapy.

- ANBL0032—Provided data for the 2015 FDA approval of ch14.18 (dinutuximab) in combination with cytokines and isotretinoin for treatment of children with high risk neuroblastoma.

- C10403—Intergroup study conducted in older adolescent and young adult patients with newly diagnosed acute lymphoblastic leukemia (ALL) successfully used a combination chemotherapy approach developed for children to improve outcome, setting a new standard of care for this population.

- Selected Phase 2 Trials Using NCI IND Agents Under the Supervision of the Investigational Drug Branch Leading to Pivotal Phase 3 Trials

  Studies conducted in the Experimental Therapeutics Clinical Trials Network (ETCTN)

  - 8799- SPRINT Trial— has established a novel standard-of-care therapy for patients with NF1-related plexiform neurofibromas (PN). The trial assessed the MEK 1/2 inhibitor selumetinib and established that this agent can lead to durable tumor shrinkage and clinical benefit for children and adolescents suffering from symptomatic PN. Results from this trial led the US FDA to recently give selumetinib FDA orphan drug designation in the treatment of NF-1 related diseases.

- 9673—First demonstration of anti-PD-1 drug (nivolumab) in squamous cell carcinoma of anal cancer which resulted in a change in National Comprehensive Cancer Network guidelines.

Studies carried out in the NCTN

- Randomized Phase 2 study (2011-2013) of combination cediranib and olaparib versus olaparib alone in ovarian cancer has led to three pivotal trials: one in platinum-sensitive (NRG GY004) and the other in platinum-refractory (NRG GY005) ovarian cancer; another trial also emerged—NRG GY012—not yet accruing, testing olaparib and cediranib in endometrial cancer.

- The randomized Phase 2 trial of cabozantinib versus sunitinib in metastatic renal cell carcinoma (RCC) led to the pivotal METEOR trial. This comparison of cabozantinib to everolimus was the basis for the 2016 FDA approval of cabozantinib in patients with advanced renal cell carcinoma who had received prior anti-angiogenic therapy.

Studies carried out in other NCI-funded networks in the CTEP research grant portfolio

- CITN-09—First demonstration of activity of anti-PD-1 agent (pembrolizumab) in Merkel-cell carcinoma. PD-1 blockade with pembrolizumab in patients with advanced disease showed an objective response rate of 56 percent and a 67 percent rate of progression-free survival at 6 months in this Phase 2 study, which is part of the Cancer Immunotherapy Trials Network (CITN). In December 2018, the drug received accelerated approval from the FDA for this cancer.

- CITN-12—First demonstration of safety of anti-PD-1 agent (pembrolizumab) in cancer patients with HIV infection, which has led to the recommendation for inclusion of HIV+ patients in immune-oncology trials.

- A Phase 1-2 study of acalabutinib (ACP-196) showed promising safety and efficacy profiles (overall response rate of 95 percent, including partial responses) in patients with relapsed chronic lymphocytic leukemia. These results led to a pivotal Phase 3 trial and FDA approval of the agent.